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DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,831	SCHWABE ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *13-19 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,20 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed 7/5/07 is acknowledged and has been entered.

The Declaration of Gerald T. Nepom under 37 CFR 1.132 filed 7/5/07 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of Group I and species of light detectable label in Applicant's said response is acknowledged.

Claims 1-12, 20 and 24-27 are currently being examined.

3. The disclosure is objected to because of the following informalities:

The use of the trademark MINIPREP has been noted in this application, for example at [0095]. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction(s) is/are required.

4. The amendment filed 7/5/07 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the originally filed disclosure is as follows:

a. The amendment at [0098] to add "This PCR product codes for a protein sequence which comprises the sequence QGQSPLGSDL GPQMLRELQE TNAALQDVRD WLRQQVREIT FLKNTVMECD ACGMQQSVRT GLPSVRP [SEQ ID NO: 24], which is identical to amino acids 21-87 of SEQ ID NO: 23."

b. The amendment at the Appendix II on page 41 to add "SEQ ID NO: 24" and its corresponding sequence.

c. The amendment at [0009] to add "The amino acid sequence of the oligomerisation domain has been disclosed by Efimov *et al.,* FEBS Letters 341:54-58 (1994), which for rat COMP reads as follows: QGQIPLGGDLAPQMLRELQETNAALQDVRELLRQQVKEITFLKNTVMECDA CGMQPARTPGLSV [SEQ ID NO: 22], corresponding to amino acid residues 21-83 of rat COMP" [underlined material added]. The Examiner notes that Efimov *et al* teach that the assembly domain of rat COMP is the N-terminal fragment of rat COMP comprising residues 20-83, not residues 21-83 (page 57 of Effimov *et al*).

Applicant is required to cancel the new matter in the reply to this Office Action.

5. The Examiner notes that the Genbank database accession #1705995 disclosed by Applicant as SEQ ID NO: 23 at [0097] is Genbank database accession # P49747, version P49747 GI: 1705995 that encodes human cartilage oligomeric matrix protein precursor (COMP) (see evidentiary reference NCBI for Genbank Accession No. P49747).

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 5 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the disclosure as originally filed is as follows:

a. In claim 5: "wherein the pentamerisation domain of COMP comprised in the second section in at least one of the chimeric proteins comprises the amino acid sequence of the first fifty-three amino acids of SEQ ID NO: 22."

b. In claim 25: "wherein the pentamerisation domain of COMP comprised in the second section in at least one of the chimeric proteins comprises SEQ ID NO: 24."

8. Claims 4 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed oligomeric MHC complex and pharmaceutical composition thereof, recited in the instant claims.

The instant claims encompass an oligomeric MHC complex wherein the oligomerising domain comprised in the second section in at least one of the chimeric proteins is derived from the pentamerisation domain of cartilage oligomeric matrix protein (COMP). There is insufficient disclosure in the specification on such an oligomeric MHC complex and pharmaceutical composition thereof.

The specification discloses that the amino acid sequence of the oligomerisation domain for rat COMP is SEQ ID NO: 22, which corresponds to amino acid residues 21-83 of rat COMP ([0009)]. However, the reference from which this information has been incorporated by reference, Efimov *et al*, teach that the assembly domain of rat COMP is the N-terminal fragment of rat COMP comprising residues 20-83, not residues 21-83 (page 57 of Effimov *et al*).

The specification does not disclose the sequence of any other COMP protein from any other species except for human COMP at SEQ ID NO: 23 at [0097], the human sequence differing from the rat COMP pentamerization domain.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

9. For the purpose of prior art rejections, the filing date of the instant claims 5, 25 and 26 is deemed to be the filing date of the instant application, *i.e.*, 2/2/04, as the parent applications have do not support the claim limitations: amino acid residues 1-53 of SEQ ID NO: 22 (claim 5), SEQ ID NO: 24 (claim 25), and SEQ ID NO: 22 (claim 26).

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-12, 20 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/21572 A1 in view of WO 98/18943 A1, Terskikh *et al* (PNAS USA 1997, 94:1663-1668, IDS reference), Muller *et al* (Meth. Enzymol. 2000, 326, pages 261-282, IDS reference), Efimov *et al* (FEBS Letters, 1994, 341: 54-48, of record) and Efimov *et al* (Proteins 1996, 24: 259-262, of record).

WO 99/21572 A1 teaches oligomeric MHC single chain (sc) class I or class II complexes comprising a first portion consisting of one or more single chain class I or class II linked or fused to a joining molecule and optionally an effector molecule, said joining molecule linking the first portion to a second such portion, said joining molecule can be a peptide tag, an IgH or IgL chain, or a coiled-coil domain. WO 99/21572 A1 further teaches that single chains of MHC can be combined to produce novel homo-or-heterodimeric MHC complexes (page 8 at the first paragraph). WO 99/21572 A1 teaches that the effector molecule can be an scFv antibody, said scFv antibody specific for the same TCR the MHC molecule is specific for or for a different molecule. WO 99/21572 A1 further teaches that the complex may comprise a label such as a radionuclide, and the sc MHC molecule may be linked to an antigenic peptide that binds

in the MHC binding groove, *e.g.,* an immunodominant peptide from MBP, type II collagen, GAD for which a T cell response exists in a patient. WO 99/21572 A1 teaches pharmaceutical compositions comprising the oligomeric MHC class II complexes (see entire reference, especially page 3 at the last paragraph, paragraph spanning pages 4-5, page 30 at lines 4-33, page 31, page 32 through line 32, page 42 at lines 11-13 and lines 22-34, page 51 at lines 6-22, page 52 at lines 8-12, figure 9, figure 10).

WO 99/21572 A1 does not teach wherein the coiled-coil domain is the COMP pentamerization domain(s) recited in the instant claims.

WO 98/18943 A1 teaches that scFv antibodies can be pentamerized using the pentamerization domain of COMP, *i.e,* by fusing the scFv to said COMP domain (a coiled-coil) with or without a linker. WO 98/18943 A1 teaches that the domain capable of binding to an acceptor, in this instance, an scFv antibody can be attached at the N- or C-terminus of the said COMP domain either directly or through a spacer, and the construct may further comprise a domain such as a marker or an enzyme or a binding domain, and the said acceptor is for example a receptor. WO 98/18943 A1 teaches that the COMP assembly domain spontaneously pentamerizes *in vitro* or *in vivo*, and since it does not depend upon disulfide bond formation, is therefore a preferred embodiment of the invention. WO 98/18943 A1 teaches that oligomerization of short peptides such as scFv antibodies bypasses folding problems and overcomes expression difficulties previously experienced during oligomerization of relatively complex proteins (see entire reference, especially page 2 at the detailed description of the invention, page 3 at the second and third full paragraphs, page 4 at the first two paragraphs, page 5 at the first two full paragraphs, claims).

Terskikh *et al* teach a pentameric antibody complex comprising the pentamerization domain of COMP, a coiled-coil assembly domain. Terskikh *et al* teach that the COMP assembly domain spontaneously forms a five-stranded α helical bundle, the highest oligomerization state know for a compact coiled-coil structure. Terskikh *et al* teach that various forms of this domain can be readily produced in *E. coli* and easily purified to near homogeneity under nondenaturing conditions. "These properties, taken together with a remarkable solubility in salt-free water (up to 20 mg/ml) and thermostability, make the COMP assembly domain an ideal pentamerization tool for protein engineering...thus....bypasses the difficulties previously encountered during the expression of oligomeric forms of relatively complex proteins...". Terskikh *et al* teach that the fusion of the protein-COMP construct to other different relevant polypeptides such as an FcR binding domain, would provide new functional properties to this molecule in addition to the multivalent high avidity binding (especially abstract, Introduction, first paragraph at column 1 on page 1664, discussion section).

Muller *et al* teach that chimeric multimers made by genetic fusions to heterologous oligomerization domains can be constructed with coiled coils that act as versatile fusion partners, having small domains with predictable quaternary structure and adjustable stability (especially first paragraph). Muller *et al* teach that the best-characterized pentamer occurs in COMP (especially page 264, last sentence at the end of the first full paragraph). Muller *et al* teach using coiled coils to generate chimeric proteins with higher avidity (especially paragraph spanning pages 267-269). Muller *et al* teach that the coiled coil can be genetically fused to the protein of interest via a flexible linker (especially first sentence on page 269). Muller *et al* teach adding fluorescent labels to the multimers, and use of the multimers for numerous biochemical, genetic, diagnostic and therapeutic applications (especially page 281 at the last two paragraphs).

Efimov *et al* (1994) teach that amino acid residues 20-83 of COMP protein can be over-expressed in *E. coli* and purified under non-denaturing conditions. Efimov *et al* teach that this fragment forms pentamers similar to the assembly domain of the native protein, and its five chains can be covalently linked *in vitro* by oxidation of cysteines 68 and 71. Efimov *et al* teach that this fragment adopts a predominantly α-helical structure as judged by circular dichroism spectroscopy (especially abstract).

Efimov *et al* (1996) teach that COMP is a pentameric glycoprotein and that self-association of COMP is achieved through the formation of a five-stranded α-helical bundle that involves amino acid residues 20-83, and the further stabilization by interchain disulfide bonds between cysteines 68 and 71. Efimov *et al* (1996) teach that COMP assembly domain has features of a coiled-coil (especially abstract and introduction section).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used as the coiled-coil domain, in the MHC-linker-coiled-coil-scFV oligomeric construct taught by WO 99/21572 A1 the coiled-coil COMP assembly domain taught by WO 98/18943 A1, Terskikh *et al*, Muller *et al*, Efimov *et al* (1994) and Efimov *et al* (1996). It would also have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made the contruct taught by WO 99/21572 A1 without the scFv since WO 99/21572 A1 teaches the scFv effector molecule is optional.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 99/21572 A1 teaches an MHC oligomeric complex containing coiled-coil domains and the advantages of using them to increase avidity of MHC complexes, Terskikh *et al* teach that the COMP assembly domain spontaneously forms a five-stranded α helical bundle, the highest oligomerization state known for a compact coiled-coil structure, and this domain can be readily produced in *E. coli* and easily purified to near homogeneity under non-denaturing conditions, and use of such domain can bypass problems encountered in the expression of oligomerized forms of relatively complex proteins, Muller *et al* teach the versatility and stability of coiled-coil

domains for oligomerizing proteins, the advantage of increased avidity that their use provides, and their use in various diagnostic and therapeutic applications, Efimov *et al* (1994) teach that amino acid residues 20-83 of COMP protein can be over-expressed in *E. coli* and purified under non-denaturing conditions, Efimov *et al* (1996) teach the location of the COMP assembly domain, that it spontaneously forms a pentameric structure and is a coiled-coil domain, and WO 98/18943 A1 teaches scFv antibodies can be pentamerized using the pentamerization domain of COMP and that because of COMP's ability to assemble spontaneously as a pentamer *in vitro* or *in vivo* since it does not depend upon disulfide bond formation, it is a preferred embodiment of the invention.

Applicant's arguments in the amendment filed 7/5/07 are moot in light of the new rejection.

However, with regard to Applicant's argument to Terskikh *et al*, also presented in the Rule 1.132 Declaration of Gerald T. Nepom (filed on the same date), it is the Examiner's position that Terskikh *et al* do not teach away from the claimed invention, and in fact offer oligomerization using COMP as a solution for bypassing the difficulties previously encountered during the expression of oligomeric forms of relatively complex proteins.

13. Claims 24, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/21572 A1 in view of WO 98/18943 A1, Terskikh *et al* (PNAS USA 1997, 94:1663-1668, IDS reference), Muller *et al* (Meth. Enzymol. 2000, 326, pages 261-282, IDS reference), Efimov *et al* (FEBS Letters, 1994, 341: 54-48, of record) and Efimov *et al* (Proteins 1996, 24: 259-262, of record) as applied to claims 1-12, 20 and 26 above, and further in view of Dinser *et al* (J. Clin. Invest. 8/15/02,110(4): 505-513), Newton *et al* (Genomics. 1994, 24: 435-439) and admissions in the instant specification at [0097]-[0098].

WO 99/21572, WO 98/18943 A1, Terskikh *et al* (PNAS USA 1997, 94:1663-1668, IDS reference), Muller *et al* (Meth. Enzymol. 2000, 326, pages 261-282, IDS reference), Efimov *et al* (FEBS Letters, 1994, 341: 54-48, of record) and Efimov *et al* (Proteins 1996, 24: 259-262, of record) have all been discussed supra, hereafter referred to as "the combined references."

The combined references do not teach using an oligomerizing domain that is derived from the pentamerization domain of human COMP, including one comprising the amino acid residues recited in claims 24 and 25.

Dinser *et al* teach that human COMP consists of an N-terminal coiled-coil domain followed by several other domains, and that its sequence was known (especially paragraph spanning columns 1-2 on page 505 and reference 17 in the bibliography).

Newton *et al* teach cloning and sequencing of human COMP, and the region that is required for pentamer formation (especially abstract and Figure 2).

The admissions in the instant specification at [0097]-[0098] are that SEQ ID NO: 23 is Genbank accession #1705995 (human COMP) and that SEQ ID NO: 24 is amino acid residues 21-87 of SEQ ID NO: 23, respectively.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the MHC class I or class II oligomeric complexes taught by the combined references by substituting the rat COMP coiled-coil domain taught by the combined references with the human COMP coiled-coil domain taught by Dinser *et al* and by Newton *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a less immunogenic construct for a pharmaceutical composition intended for humans, as the combined references, particularly WO 99/21572 A1 teaches that the constructs may be made with human class I or class II MHC molecules (paragraph spanning pages 49-50), and Dinser *et al* and Newton *et al* teach the corresponding human COMP coiled-coil domain region.

The instant claims are included in this rejection because SEQ ID NO: 24 recited in instant claim 25 is a subsequence of human COMP corresponding to amino acid residues 21-87 of SEQ ID NO: 23, human COMP, recited in instant claim 24.

14. Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/070725 A1 in view of WO 99/21572 A1.

WO 02/070725 A1 teaches that the multimerization domain of COMP or TSP-5 is a coiled coil domain and can be used to make a chimeric protein of the invention. WO 02/070725 A1 teaches that such conjugates can be made by a conjugation of the multimerization domain of COMP and any protein or amino acid drug, including ones derived from human proteins (especially paragraph spanning pages 15-16, page 16 at the first full paragraph). WO 02/070725 A1 teaches that the chimeric proteins can have the structure of the pentamers comprising the multimerization domain of human COMP, a spacer, and a protein or amino acid drug or pentamers comprising a specific amino acid domain to a specific site of action, a spacer, the multimerization domain of human COMP, a spacer and a protein or amino acid drug, and wherein the chimeric protein arms of different types are joined at the COMP multimerization domain. WO 02/070725 A1 teaches that the multimerization domain of COMP is amino acid residues 1-88 (especially Examples III and IV, claims and figures).

WO 02/070725 A1 does not teach wherein the COMP is the coiled-coil domain in an MHC oligomeric complex.

WO 99/21572 A1 teaches oligomeric MHC single chain (sc) class I or class II complexes comprising a first portion consisting of one or more single chain class I or class II linked or fused to a joining molecule and optionally an effector molecule, said joining molecule linking the first portion to a second such portion, said joining molecule can be a peptide tag, an IgH or IgL chain, or a coiled-coil domain. WO 99/21572 A1 further teaches that single chains of MHC can be combined to produce novel homo-or-heterodimeric MHC complexes (page 8 at the first paragraph). WO 99/21572 A1 teaches that the effector molecule can be an scFv antibody, said scFv antibody specific for the same TCR the MHC molecule is specific for or for a different molecule. WO 99/21572 A1 further teaches that the complex may comprise a label such as a radionuclide, and the sc MHC molecule may be linked to an antigenic peptide that binds in the MHC binding groove, *e.g.,* an immunodominant peptide from MBP, type II collagen, GAD for which a T cell response exists in a patient. WO 99/21572 A1 teaches pharmaceutical compositions comprising the oligomeric MHC complexes (see entire reference, especially page 3 at the last paragraph, paragraph spanning pages 4-5, page 30 at lines 4-33, page 31, page 32 through line 32, page 42 at lines 11-13 and lines 22-34, page 51 at lines 6-22, page 52 at lines 8-12, figure 9, figure 10).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed an oligomeric protein complex such as taught by WO 02/070725 A1 comprising the human COMP pentamerization domain taught by WO 02/070725 A1, including the MHC class I or class II complexes or chains taught by WO 99/21572 A1 and optionally also including an scFv antibody as taught for the oligomeric coiled-coil complexes of WO 99/21572 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 02/070725 A1 teaches that the multimerization domain of COMP or TSP-5 is a coiled coil domain that can be used to make a chimeric protein containing one or two protein or peptide drugs or specific amino acid domains to specific sites of action, and WO 99/21572 A1 teaches MHC class I or class II coiled-coil multimers, optionally also containing scFv effectors, and their usefulness as pharmaceuticals.

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1-12, 20 and 24-27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 and 29 of copending Application No. 10/770,140. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '140 are encompassed by the instant claims.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record on page 14 of the amendment filed 7/5/07.

It is the Examiner's position that the instant claims are under rejection.

17. Claims 1-12, 20 and 24-27 are directed to an invention not patentably distinct from claims 1-26 and 29 of commonly assigned 10/770,140 as enunciated supra.

18. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 10/770,140, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

19. Claims 1-12, 20 and 24-27 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0074848 A1 (publication of commonly assigned 10/770,140).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

US 2005/0074848 A1 discloses the oligomeric MHC complex and pharmaceutical composition thereof recited in the instant claims (see entire document, especially claims).

The instant claims "comprise" the recited components.

20. Claim 3 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 2. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

21. Claims 6, 8 and 10 are objected to because of the following informalities:

There are misspellings in the claims, "do-main" in claim 6 at line 3, "comple-mentary" in claim 8 at line 2, and "substan-tially" in claim 10 at line 2.

Appropriate correction is required.

22. No claim is allowed.

23. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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